REMARKS

Status of Claims

Claims 3-5, 7, 9-12, 14-15, 18, and 20-21 are pending in this application. Claims 1-2, 6, 8, 13, 16-17, and 19 have been canceled in this amendment. Claims 3-5, 9-10, 12, 14-15, 18, and 20-21 have been amended to more particularly point out and distinctly claim that which the applicants regard as their invention. Support for the claim amendments can be found, *inter alia*, in the original claims. No new matter has been added by these amendments.

Claim Rejections under 35 U.S.C. § 112

The rejection of claims 1-2, and 12-14 under 35 U.S.C. § 112, second paragraph, as being incomplete for omitting essential steps, is believed overcome by the amendments to the claims. Specifically, claims 1-2, and 13 have been cancelled, and claim 3 has been amended to incorporate the subject matter of cancelled claims 1 and 2.

The rejection of claim 4 under 35 U.S.C. § 112, second paragraph, is also believed to be overcome in light of the amendments to claim 4. The claim has been amended to correct the numbering of the steps, and to correct the lack of antecedent basis for "the selected cells".

The rejection of claims 15-21 under 35 U.S.C. § 112, second paragraph, is believed to be overcome in light of the amendment to claim 15. The Office has objected to the term "substantially pure" in the claim, and therefore the term has been removed from the claim.

Claim Rejections under 35 U.S.C. § 102

The rejection of claims 1-3, 5-7, 11-12, and 15 under 35 U.S.C. § 102(b) as being anticipated by Collins et al. (2001), J. Cell Science, Vol. 114, 3865-3872 (hereinafter "Collins (2001)") is respectfully traversed.

The presently claimed invention is directed to a method of isolating prostate cancer stem cells which express the CD133 antigen and high levels of $\alpha_2\beta_1$ integrin. The claimed method starts with a population of prostate *cancer* stem cells, and

proceeds by binding the prostate cancer stem cells to a collagen matrix, and selecting the cells that express the CD133 antigen.

In contrast, Collins (2001) teaches a method for isolating a population of prostate stem cells, where the original population of prostate cells is non-cancerous. The method in Collins (2001) selects prostate stem cells based on the expression of CD44. Collins (2001) is silent on the use of CD133 antigen as a marker for prostate *cancer* stem cells.

The Office Action asserts that while the reference does not disclose the testing of the prostate stem cells for the expression of the CD133 antigen, the expression of the CD133 antigen by these stem cells is an inherent characteristic. Applicants respectfully disagree with this assertion, and submit an additional Collins reference as evidence to the contrary (see attached Collins et al. (2005), Cancer Res., 65(23): 10946-51; hereinafter "Collins (2005)"). The Collins (2005) reference shows that it is possible to obtain cells that express CD44, and that do ***not*** express CD133 (see Figure 1A, page 10948). Therefore, it cannot be said that when one isolates prostate stem cells based on CD44 expression, following the method described in the cited reference, they will be left with a population of cells that ***both*** express CD44 and CD133. And further, it cannot be concluded that the expression of CD133 is an inherent characteristic of cells that express CD44.

The cited reference starts with a different population of cells and selects for a different marker in that population, and as discussed above, selection for that CD44 marker does not inherently isolate cells that express CD133, and therefore the presently claimed method is not anticipated by the teaching of Collins (2001). Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection.

Claim Rejections under 35 U.S.C. § 103

The rejection of claims 8-10, 13-14, and 16-21 under 35 U.S.C. 103(a) as being obvious over Collins (2001), in view of Mangano (US 2007/0134794) is respectfully traversed.

As discussed above, the presently claimed invention is directed to a method of isolating prostate cancer stem cells by selecting cells that express the CD133 antigen. Collins (2001) is cited for its disclosure of a method of isolating prostate stem cells based on the selection of CD44 expression. Mangano is cited for its teaching of methods of selecting for and enriching stem cells. While Mangano describes the isolation of prostate stem cells from sources such as solid tumors or metastatic tissue, Mangano does not disclose a method of isolating prostate cancer stem cells based on the CD133 marker.

In fact, the Office Action concedes that neither Collins (2001) nor Mangano teach that prostate cancer stem cells express CD133 antigen (page 9 of Office Action). And, as detailed above, the Office Action erroneously concludes that the expression of CD133 is an inherent characteristic of prostate stem cells isolated using the Collins (2001) method.

All that we know about the prostate stem cells isolated using the method described in Collins (2001) is that they express CD44. It is impossible to tell whether or not these cells isolated from benign tissue also express CD133. This is demonstrated by the Collins (2005) reference which shows that it is possible to have cells that express CD44 and do not express CD133. In other words, the expression of CD133 is not an inherent characteristic of cells that express CD44.

Additionally, the Applicants have found that cells that do express CD133 have several unique characteristics that are not disclosed in Collins et al. or Mangano. For example, prostate cancer stem cells that express CD133 have enhanced colony forming activity as compared to cells that do not express CD133 (see Figure 1b). Also, prostate cancer stem cells that express CD133 isolated from a lymph node metastasis have a greater capacity to invade (see Figure 2b). And additionally, prostate cancer stem cells that express CD133 have the ability to form tumors in a xenograft model (see Figure 1c).

As further evidence of the unique characteristics of the prostate cancer stem cells that express CD133, described above, Applicants again point to Collins (2005). Collins (2005) illustrates that cells that express CD133 cells and have high levels of $\alpha_2\beta_1$, and express CD44, have increased colony forming capacity as compared to

cells that express CD44 and have high levels of $\alpha_2\beta_1$ but ***do not express*** CD133 (Figure 1A). Collins (2005) also shows that cells that express CD133 have increased proliferation when compared to cells that do not express CD133 (Figure 1B). Additionally, cells that express CD133 cells have enhanced invasive properties (Figure 2A); and greater survival (Figure 2B).

Because the cited references do not describe a method of isolating prostate cancer stem cells based on the expression of the CD133 antigen, and the properties described above are ***not*** inherent from the teachings of the cited references, one of skill in the art would not have arrived at the present invention by combining the teachings of the cited references. Accordingly, the combined disclosure of Collins (2001) and Mangano do not render the present invention obvious, and reconsideration and withdrawal of the rejection are respectfully requested.

Conclusion

The application is respectfully submitted to be in condition for allowance, and prompt, favorable action thereon is earnestly solicited.

If there are any questions regarding this reply or the application in general, a telephone call to the undersigned at (202) 624-2845 would be appreciated since this should expedite the examination of the application.

If necessary to effect a timely response, this paper should be considered as a petition for an Extension of Time sufficient to effect a timely response, and please charge any deficiency in fees or credit any overpayments to Deposit Account No. 05-1323, Docket No. 100846.59603US.

Respectfully submitted,

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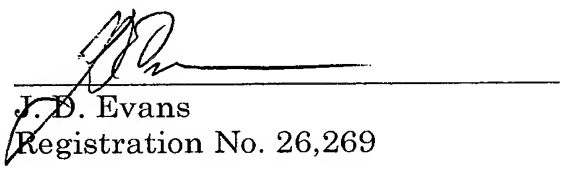

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